

EDITORIAL

Surgery of Sarcomas in the Multimodality Era

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The interesting study by Rossi et al. [1] in this issue deals with the topic of local recurrence, which correlates highly with the presence of microscopically positive margins. Due to the large size of many of the specimens in many sarcoma series and the labor involved in a thorough pathologic evaluation and documentation of the microscopic status of the surgical margins, this important piece of information is often missing.

Local recurrence is of major concern to the surgeons because it signifies failure of the surgical treatment, along with the failure of other adjuvant modalities when the latter are used. Local recurrence presents a substantial morbidity for the patient requiring further local treatment and, for this reason alone, it should be avoided. Whether local recurrence is the cause in itself of distant dissemination and increased mortality for these patients is debatable. In some series of patients with local recurrence of extremity sarcoma, the survival following treatment of the local recurrence is about the same as that of patients with primary sarcomas. This may be partly due to a selection of patients, that is, in a series of patients with local recurrence alone, in which patients with local recurrence and distant metastases are excluded, the average composition of the grade of the tumors involved tends to be lower than that of a group of patients with primary sarcomas. This may compensate for whatever adverse effect on survival a local recurrence may have.

Perhaps a better way to evaluate the effect of local recurrence on survival is to consider local recurrence as a possible prognostic indicator of survival in a multivariate analysis of a series of primary soft tissue sarcomas. In a large series from Memorial Sloan-Kettering Cancer Center (MSKCC) concerning primary extremity sarcomas, local recurrence was strongly associated with the development of metastasis and disease-specific death, on multivariate analysis [2]. The issue is more complicated, however, because one should distinguish between a single event of a treatable local recurrence and that of a repeated local recurrence that finally becomes uncontrollable. Anatomic location of the primary tumor certainly is important

in affecting the possibility of local control and survival. Extremity locations are more easily controllable than torso locations, particularly retroperitoneal lesions where local recurrence is more often accompanied by the ultimate demise of the patient.

In another report from MSKCC, patients with a radical re-resection at their center (following removal of the primary tumor at another hospital) had better survival compared to patients who had the primary tumor removed at their own center [3]. Similar results were observed in our experience in the Roswell Park series [4]. This signifies that a second resection should be applied liberally to patients referred to a tertiary center following local excision of a primary tumor at a primary hospital, and also, that a wide resection should be applied the first time, when feasible, in both primary and tertiary care settings. The improved survival of patients operated on twice is probably due to their having smaller tumors to begin with (hence the first resection at the primary center), allowing a wider margin at a second intervention, and probably to their having less aggressive tumors, thereby allowing their diagnosis when they are smaller in size.

Whatever the precise impact of local recurrence on survival, we may all agree that biologic determinants of the primary lesion (e.g., tumor grade, size, deep location) primarily determine the rate of distant recurrence and survival, but that occasionally local recurrence in certain anatomic locations may result in the demise of the patient.

In the series by Rossi et al. [1], all patients with narrow margins received multimodality treatment consisting of regional perfusion and/or adjuvant radiation. The local recurrence rate in these patients was 22%. In the Roswell Park series, this rate was 25% for patients with local excision and adjuvant radiation [4]. In the prospective

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randomized study by Brennan et al. [5], the group of surgery plus brachytherapy had a significantly lower local recurrence rate than that of surgery alone, but patients in the nonrandomized portion of the study treated with surgery plus radiation had a local recurrence rate of ~30% [5]. In another report from the same institution concerning sarcomas shaved off major vessels or nerves treated with brachytherapy, the local recurrence rate was also 30% [6]. In our series, ~75% of the patients with extremity sarcomas in whom an adequate surgical margin was obtained, the local recurrence rate was 10%, whereas in patients with close surgical margins and adjuvant radiation this was 25% [4]. These results indicate that adjuvant radiation administered in patients with potential microscopic residual eradicates the latter in ~70% of the patients. However, it is not a panacea and its role for the local control of retroperitoneal sarcomas has not been established [7].

The association between positive surgical margins and increase in local recurrence signifies that a wider margin should help improve local control rates. A wider margin may not be possible in certain anatomical areas, e.g., in the distal portions of the extremities where the distance between the skin and underlying bones is so small, but in most other areas it is often feasible. The role of limb-sparing surgery in the context of multimodality treatment, attaining limb preservation rates in excess of 90%, requires more surgical skill than amputation since it must optimally combine the twin goals of negative surgical margins and the preservation of important functions. The concept of en bloc resection of the biopsy incision with the underlying tumor and of resection of an involved muscle from near the origin to insertion should be applied. Most tissues around a sarcoma mass have no great functional significance and, therefore, can be widely resected, restricting the margin only in the vicinity of functionally important structures. In the latter case, entering the sheath of a major nerve adjacent to the tumor, or removing en bloc the periosteum of the adjacent bone, helps improve the margin. If necessary, a nerve may be sacrificed (in preference to an amputation) or a segment of bone or major vessel followed by reconstruction. The functional muscular reserve of the extremity is considerable so that wide resections are accompanied by little or no functional sequelae for ordinary activities. In the proximal lower extremity, resection of the buttock, the posterior or medial compartment, or a modified anterior compartment resection cause no major problems in ambulation [8].

In conclusion, the surgical treatment of primary sarcomas remains the primary treatment in the multimodality

setting. Its quality should not be compromised or relaxed because of the use of other adjuvant modalities, which, at present, although fairly effective, are not universally so in eradicating microscopic residual disease.

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COMMENTARY

Positive microscopic margins on surgical resection specimens of cancers have uniformly been found to be associated with poorer clinical outcomes, even if adjuvant radiation is employed. Breast cancer and soft tissue sarcoma of the extremities are two primary types of cancer receiving special attention in this regard, due to an understandable recent interest in more conservative operations for these conditions.

Dr. Karakousis has effectively summarized the clinical data that demonstrate there is no substitute for microscopically clear margins when limb-sparing operations are utilized for soft tissue sarcoma. This was the conclusion also of the 1985 National Institutes of Health Consensus Conference on Limb Sparing Surgery for Sarcomas. Dr. Bernard Gardner will summarize similar data for breast cancer in a coming editorial in this journal. Adjuvant radiation is clearly beneficial for both these cancers and others, but is abundantly clear that adequate surgical resection with clear microscopic margins must remain the "order of the day" for all cancers treated by operation.

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